REMARKS

Applicants submit this response to the Office Action dated July 19, 2005. Claims 15-18 are pending, and claim 15 is amended as discussed below. No new matter is added.

The first Office Action (mailed May 25, 2004) rejected claims 15-18 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. This ground of rejection was fully withdrawn in the second Office Action (January 31, 2005). The claims have not been amended since applicants responded to the first Office Action.

The only issue raised in the second Office Action (mailed January 31, 2005), was a 35 U.S.C. § 102(e) rejection over Agarwal. Applicants have overcome this rejection and it has now been withdrawn. Thus, applicants relied on that rejection being the only outstanding substantive ground to address prior to allowance of the claims.

It is unclear why the present, third, non-final Action again presents a rejection under 35 U.S.C. § 112, first paragraph, when this ground of rejection has been thoroughly addressed. The Examiner has not responded in detail to Applicants' arguments dated November 24, 2004, but these arguments must have been persuasive in that the rejection was withdrawn on January 31, 2005.

However, in order to advance the prosecution, applicants have addressed herein the current rejections under 35 U.S.C. § 112, first paragraph.

Claims 15-18 are rejected under 35 U.S.C. § 112, first paragraph, as the specification allegedly is not enabling for the genus of epitopes of SEQ ID NO:4. Applicants respectively submit that the claims as amended are enabled under the standards set forth in Wands as provided by the Examiner.

A specification is presumed to be enabling and the U.S. Patent and Trademark Office (PTO) has the burden of establishing a *prima facie* case of lack of enablement. See, In re Angstadt, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976); In re Marzocchi, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971). To make a *prima facie* case of lack of enablement, the PTO must come forward with reasons, supported by the record as a whole, showing why the specification fails to enable one of ordinary skill in the art to make and use the claimed invention. In re Angstadt, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976). The mere fact that some experimentation is necessary does not negate

enablement as long as undue experimentation is not required. See M.P.E.P. § 608.01(p).

The burden is on the PTO to establish that experimentation would be undue, Angstadt, 190 U.S.P.Q. at 219, taking into consideration the eight factors that are to be considered in determining whether a disclosure requires undue experimentation. In re Wands, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Applicants submit that the amount of experimentation which may be required to practice the present invention does not rise to the level of being undue experimentation, as defined by the Court in Wands.

An important aspect of the Court's decision in Wands is its finding that the nature of the technology pertinent to the Wands invention (monoclonal antibody production) permitted a broad definition of the term "experiment." The Court found that an "experiment" in the monoclonal antibody art consisted of the entire attempt to make a monoclonal antibody against a particular antigen. As described by the Court, the process entailed, "immunizing animals, fusing lymphocytes from the immunized animals with myeloma cells to make hybridomas, cloning the hybridomas, and screening the antibodies produced by the hybridomas for the desired characteristics." 8 U.S.P.Q.2d at 1407. Thus, Wands supports the conclusion that in, a complex field such as monoclonal antibody production, the entire attempt to achieve the desired result, from beginning to end, constitutes one experiment.

According to the Court, repetition of this whole experiment more than once does not constitute undue experimentation. As the Court indicated, practitioners in the art would be prepared to screen negative hybridomas in order to find a hybridoma making the desired antibody. 8 U.S.P.Q.2d at 1406. Thus, the fact that some aspects of the experiment as a whole may yield negative results does not mandate a finding that the experimentation to achieve a positive result is undue.

Like the production of monoclonal antibodies, the identification or production of a epitope having the limitations of the present claims may require some experimentation, but if viewed in the light of Wands, this experimentation, and the possibility of encountering negative results along the path to the positive results, is not undue. Furthermore, the present applicants provide extensive guidance to allow one of ordinary skill in the art to obtain a polypeptide that is within the scope of the claims.

The inventors have, for the first time, identified and sequenced a human protein referred to as SEQ ID NO:4. The Examiner previously indicated that this sequence, and the epitopes of SEQ ID NO:7 and 8 were free of the art. The remaining epitopes are also free of the art of record, as indicated by the withdrawal of the previous rejection of claims 15-18 under 35 U.S.C. § 102(e).

Applying this information to the eight Wands factors, one of skill in the art would conclude that undue experimentation would not be required to practice the claimed invention.

1. *The breadth of the claims.* Using materials and methods routinely available at the time of filing, one of skill can routinely identify or construct any polypeptide molecule meeting the limitations of the claims, and based on the protein of SEQ ID NO:4. Claims 15-18 as amended herein recite the functional limitation of use for producing an antibody that binds to the polypeptide of SEQ ID NO:4, as suggested by the Examiner at page 4, lines 12-13, of the Office Action.

2. *Nature of the invention and the state of the prior art.* The invention relates to human polypeptides. Methods of synthesizing and expressing polypeptides, and production and testing of antibodies, form a basis for the biotechnology industry. The nature of the invention is such that it is well-known to those of ordinary skill in the art. The court in Wands stated that the nature of monoclonal antibody technology is that it involves screening, including screening of negative samples (in that case, hybridomas). The number of potentially negative samples was not viewed as a determining factor in reaching a finding of undue experimentation (8 USPQ 2d at 1406-1407).

The prior art provides the methods and materials needed to apply these methods to this group of polypeptides, specifically epitopes of SEQ ID NO:4. The Wands court found that "all the methods needed to practice the invention were well-known." (8 USPQ 2d at 1406). Similarly, the methods of measuring protein binding to antibodies, and determining amino acid sequences, are well known. The Examiner noted that several members of the FGF family exist, and that an antibody to an epitope may bind to a homologue of the polypeptide or to a different polypeptide. Applicants submit that claims 15-18 as amended herein address these factors.

3. *Amount of direction or guidance provided and the existence of working examples.* The specification provides clear directions for performing the experimentation, and cites to published scientific articles for details not mentioned in the specification. Similarly, the Wands court found that the starting material was available to the public (and the present application discloses the sequence of SEQ ID NO:4) and the patent at issue in Wands provided a detailed description of the methods, which included use of a commercially available kit. (8 USPQ 2d at 1404, 1405). The epitopes claimed in the present application are based on the disclosed SEQ ID NO:4. The specification describes production of antibodies using an epitope of the invention, at page 36, lines 5-15.

4. *The relative skill in the art, the predictability or unpredictability in the art, and the quantity of experimentation necessary.* To determine if an epitope falls within the scope of the claims, the only experimentation required is the performance of known antibody binding procedures. These procedures are routine and would not have to be done repeatedly before a definitive result was obtained. Because the inventors and the art provide means for the objective measurement of an epitope falling within the claim scope, this factor is met, for example, by the ability of the SEQ ID NO:4 to bind to an antibody raised against an epitope. This is described in the specification at page 25, lines 3-25.

The Wands court found that practitioners in the art are prepared to screen negative hybridomas to find one that made the desired antibody. (8 USPQ2d at 1406.) The court further stated that an "experiment" was not simply the screening of a simple hybridoma, but instead was the entire attempt to make a monoclonal antibody against a particular antigen. This process included immunizing animals, fusing lymphocytes from the immunized animals to make hybridomas, cloning the hybridomas, and screening the antibodies produced by the hybridomas. (8 USPQ2d at 1406).

By analogy, a single experiment in the present art could include obtaining or constructing an epitope, raising antibodies, and testing the antibodies for binding to a protein of SEQ ID NO:4. Encountering negative results would not mean that undue experimentation is involved, according to Wands.

Those of skill in this art are highly skilled and would be competent at designing and performing, or directing the performance of, the procedures described in this section. The Wands court found that the level of skill in the monoclonal antibody art was high at the time the application was filed, but, importantly, the court found that development of skill in performing specific experiments relevant to the art did not preclude enablement. Specifically, the court stated that initial failures occurred as the inventors learned to fuse cells, and "[o]nce they became skilled in the art, they invariably obtained numerous hybridomas ..." that met the claim limitations. (8 USPQ 2d at 1406.) By analogy, it would not defeat enablement for one of skill in the art of antibody production and assays to learn and become proficient in techniques for practicing the present invention.

One of skill, being acquainted with the methods described in the application, would understand that when a polypeptide of SEQ ID NO:4 specifically binds to an antibody raised against an epitope as claimed, the epitope will fall within the scope of the claims.

In Wands, the Court noted that the cell fusion technique was well known to those of ordinary skill in the art, and that there was no indication that the fusion step should be more difficult or unreliable for the antigen in question (HBsAg) than for other antigens. The Examiner has provided no evidence that the antibody binding and amino acid sequencing steps would be "more difficult or unreliable" (8 USPQ2d at 1406) than for SEQ ID NO:7 and 8.

In view of the foregoing remarks, applicants submit that the Examiner has not met his burden of making a *prima facie* showing that undue experimentation is required in order to practice the invention as claimed. Reconsideration and withdrawal of this rejection are respectfully requested.

Claims 15 and 16 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey that the inventors had possession of the claimed invention at the time of filing. Reconsideration and withdrawal of this rejection are respectfully requested. Claim 15 has been amended to recite a biological activity, which addresses

the Examiner's concerns at page 7, third paragraph, of the Office Action. The amendment is supported, for example, at page 2, lines 1-4, and page 27, lines 15-22.

Applicants traverse this rejection on the grounds that by disclosing a polypeptide sequence (SEQ ID NO:4), and representative epitopes (SEQ ID NO:7 and 8), applicants have disclosed the features of the genus of epitopes of SEQ ID NO:4. The application therefore provides written description of the SEQ ID NO:4 epitopes as claimed in claims 15 and 16.

In support of the rejection, the Examiner stated that the specification must provide sufficient distinguishing identifying characteristics of the genus.

The goal of the written description requirement is to prevent applicants from claiming priority to earlier applications if the current application discloses new matter not present in the earlier applications (Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). Further, In re Kaslow affirms that "the test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at the time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language" (707 F.2d 1366, 1375 (Fed. Cir. 1983)). The Examiner may have misapplied the written description requirement in this case. While the current application is divisional of an earlier application, the claimed subject matter is fully supported by the specification of the current application, and the law does not require the applicant to demonstrate literal support in the specification for epitopes of SEQ ID NO:4. By providing the written amino acid sequence and exemplary epitopes (SEQ ID NO:7 and 8), one of skill would know that applicants were in possession of epitopes of this sequence at the time of filing. See, for example, page 26, lines 4-7, which discloses the use of an amino acid sequence "of all or part of the protein." As the protein of SEQ ID NO:4 is provided and described, parts thereof are also provided and described.

The present claim language is consistent with claim language related to epitopes as presently allowed by the U.S.P.T.O. See, for example, U.S. Patent No. 6,908,987, in which claim 5 recites:

> An isolated antigenic peptide of PGC-1 comprising at least 8 contiguous amino acid residues of the amino acid sequence shown in SEQ ID NO:2, the peptide comprising an epitope of PGC-1 such that an antibody raised against the peptide forms a specific immune complex with PGC-1. (Emphasis added.)

For the foregoing reasons, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph (written description) is respectfully requested.

Commissioner is hereby authorized to charge the required fees of $450, to Deposit Account No. 04-0258. If additional fees are believed necessary, the Commissioner is further authorized to charge any deficiency or credit any overpayment to Deposit Account No. 04-0258.

All of the claims remaining in the application are now believed to be allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

If questions remain regarding this application, the Examiner is invited to contact the undersigned at (206) 628-7650.

Respectfully submitted,
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